

PATENT COOPERATION TREATY

REC'D 27 APR 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) **22 APR 2005**

FOR FURTHER ACTION
See paragraph 2 below

Applicant's or agent's file reference

96700/939

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US04/40852

07 December 2004 (07.12.2004)

12 December 2003 (12.12.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 38/00 and US Cl.: 514/12

Applicant

ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA U

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/40852

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/40852

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-71</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-71</u>	NO
Industrial applicability (IA)	Claims <u>1-71</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-71 lack an inventive step under PCT Article 33(3) as being obvious over Deacon et al. (Am J Physiol Endocrinol Metab, 2002) in view of Vincent et al (Ann. N. Y. Acad. Sci, 2002). Deacon et al. beneficially teach a method of inhibiting hyperglycemia-induced or free fatty acid-induced reactive oxygen formation in a mammalian cell, the method comprising treating the cell with a pharmaceutically acceptable composition comprising GLP-1 (9-36) sufficient to inhibit the hyperglycemia-induced or free fatty acid-induced reactive oxygen formation in the cell (see, e.g., abstract and page E878).

Deacon et al. do not specifically teach inhibiting reactive oxygen formation by administration of GLP-1 (9-36).

Vincent et al. teach that increased concentrations of glucose rapidly induce production of reactive oxygen species (ROS) (see, e.g., page 379, paragraph 1).

Therefore inhibiting reactive oxygen formation is considered an intrinsic effect of the anti-hyperglycemic compound GLP-1-(9-36) beneficially taught by Deacon et al.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such method of inhibiting hyperglycemia (i.e., reducing blood glucose) (e.g., using different reactive oxygen indicators, combining with other treatments and/or utilizing analogs of GLP-1-(9-36)) based upon the overall beneficial teachings provided by Deacon et al. and Vincent et al. These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Claims 1-71 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.